

THE IMPACT COURSE INTRANASAL ADMINISTRATION LOW DOSES OF DALARGIN ON THE DYNAMICS OF THE LEVEL OF AVERAGE WEIGHT MOLECULES IN BLOOD SERUM LABORATORY RATS SUBJECTED TO STRESS ULCEROGENESIS

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The work studied the impact course intranasal application low doses of dalargin on the dynamics of the content of average weight molecules in blood serum laboratory rats in normal and stress-induced ulcerogenesis.

The experiments were performed on 32 male rats weighing 180–220 g, which were divided into 4 groups. Rats in the control group (n=8) and in group II (n=8) was administrated within 28 days intranasally 0.1 ml of physiological solution (0.9-% NaCl). Animals of groups I (n=8) and III (n=8) received intranasally 0.1 ml of Dalargin (0.2mg/kg) within 28 days. On day 28 the animals of groups II (n=8) and III (n=8) were subjected to stress ulcerogenesis. Stress reaction "stress ulcerogenesis" was modeled on experimental animals in the model of forced swimming in the pool for 60 min. the Animals that were not exposed to stress ulcerogenesis in accordance with the plan of the experiment (control group and experimental group I) at this time remained in their cages. For 24 h before stress exposure in animals of all groups were not fed, leaving free access to water. Pool was represented by a ceramic tank with dimensions 80 x 80 x 130 cm water Level in it was 30 cm and the water temperature is + 20 ° C. The slaughter of experimental animals was carried out after 30 min. after stress-induced ulcerogenesis (2 hours since the introduction of the substances) by decapitation on the guillotine. Blood was collected in vacutainer tubes with a separator gel for serum BD Vacutainer®.

Material for the study was blood serum, obtained by centrifugation twice for 10

minutes at 1300 g at 25°C. Examine the levels of average weight molecules (AWM) in the blood serum using the method Gabrielian by deproteinization of 20 % trichloroacetic acid, centrifugation at 3000 g for 20 minutes and further measurements of extinction of the supernatant in the ultraviolet region of the spectrum at wavelengths (λ) of 254 and 280 nm on a spectrophotometer 5400-UV ("Ekros-Analitika", Russia). Also determined the index of distribution of AWM at the wavelengths registration of 254 and 280 nm ($ID_{280/254}$), which was calculated as the ratio of AWM extinction at the wavelengths of 254 and registration 280 nm.

Statistical processing of experimental results was performed using parametric student's t-test as the experimental data obeyed the normal distribution. Graphical visualization of data performed in the software package GraphPad Prism 6. The adopted level of significance of intergroup differences was 5 %.

It is shown that after a 28-day course intranasal administration of dalargin (0.2 mkg/kg) in blood serum of rats ($n = 8$) there was a significant decrease in the level of AWM (54,38 % at $\lambda = 254$ nm, $p \leq 0.01$; 79 % at $\lambda = 280$ nm, $p \leq 0.01$) compared with the control group ($n = 8$).

Established that in the group of rats ($n = 8$), subjected to stress ulcerogenesis after intranasal pre-course 28-day administration of 0.1 ml saline (0.9 % NaCl) showed a significant reduction in the AWM (26 % at $\lambda = 254$ nm, $p \leq 0.05$; 54,65 % at $\lambda = 280$ nm, $p \leq 0.01$) compared with the control group ($n = 8$).

It is noted that in the group of rats ($n = 8$), subjected to stress ulcerogenesis, after a preliminary course of intranasal 28-day administration of dalargin in a dose of 0.2 mkg/kg was non-specific decrease a level of AWM almost at the same level at all wavelengths registration (80,66 % at $\lambda = 254$ nm, $p \leq 0.01$; 78,32 % at $\lambda = 280$ nm, $p \leq 0.01$) compared with the control group ($n = 8$).

It is shown that in the blood serum of laboratory rats after exposure to $ID_{280/254}$ dalargin was significantly reduced by 54 % ($n = 8$; $p \leq 0.01$) compared to control, under the influence of stress ulcerogenesis ($n = 8$; $p \leq 0.01$) – 38,73 %. With the combined effects of stress ulcerogenesis and dalargin the index almost back to the values of the control group and slightly higher, amounting to 112 % ($n = 8$; $p \leq 0.01$). These results showed that a preventive course of 28-day intranasal introduction of dalargin (0.2 mkg/kg) in conditions of exposure to stress ulcerogenesis led to a return to normal ratios of the AWM, reflecting the regulatory flow ($\lambda = 280$ nm) and pathological processes in the organism ($\lambda = 254$ nm) and AWM, showing the activity of stress-realizing ($\lambda = 254$ nm) and stress-limiting systems of the organism ($\lambda = 280$ nm), providing a stress-protective effect.

Keywords: average weight molecules, stress ulcerogenesis, dalargin, low doses, intranasal administration, laboratory rats, blood serum.

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